In the Specification

Please replace the paragraph beginning on page 6, line ~~13~~ 12 with the following amended paragraph: 5/5/08 T.T.

The mammalian cell may be any type of cell other than an antigen presenting cell. In one embodiment the mammalian cell is a tumor cell. Preferable the MHC class II HLA-DR ligand is administered to the tumor cell *in vivo* in an amount effective for causing cell lysis of the tumor cell. When the mammalian cell is a tumor cell, however, in some embodiments the MHC class II HLA-DR inducing agent does not include ADRIAMYCIN™ and gamma interferon. In other embodiments when the mammalian cell is a tumor cell the MHC class II HLA-DR inducing agent does not include ADRIAMYCIN™ and gamma interferon.

Please replace the paragraph beginning on page 7, line ~~18~~ 17 with the following amended paragraph: 5/5/08 T.T.

The mammalian cell may be any type of cell other than an antigen presenting cell. The mammalian cell is a tumor cell in another embodiment. Preferably the MHC class II HLA-DR ligand is administered to the tumor cell *in vivo* in an amount effective for causing cell lysis of the tumor cell. When the mammalian cell is a tumor cell, however, the MHC class II HLA-DR inducing agent does not include ADRIAMYCIN™ and gamma interferon.

Please replace the paragraph beginning on page 7, line ~~29~~ 28 with the following amended paragraph: 5/5/08 T.T.

The MHC class II HLA-DR inducing agent is any agent which induces expression of MHC class II HLA-DR on a cell surface. Preferably the inducing agent is selected from the group consisting of ADRIAMYCIN™, gamma interferon, bacterial byproducts such as lipopolysaccharides, mycobacterial antigens such as BCG, a UCP expression vector, a TCR$\alpha\beta$ engagement molecule and a fatty acid. Once the MHC class II HLA-DR is expressed on the surface of the cell an MHC class II HLA-DR ligand can interact with the MHC class II HLA-DR and

initiate cell lysis. Preferably the MHC class II HLA-DR ligand is selected from the group consisting of an anti-MHC class II HLA-DR antibody, CD4 molecules, αβ T cell receptor molecules, γδ T cell receptor molecules and a MHC class II HLA-DR binding peptide.

Please replace the paragraph beginning on page 8, line 11 with the following amended paragraph: 5/5/08 T.T.

In another aspect the invention is a method for inducing cell lysis in a tumor cell by contacting a tumor cell with an amount of an MHC class II HLA-DR inducing agent effective to induce the expression of MHC class II HLA-DR on the surface of the tumor cell in the presence of an MHC class II HLA-DR ligand. Preferably the MHC class II HLA-DR ligand is an MHC class II HLA-DR expressing cell. In one embodiment the inducing agent is selected from the group consisting of ADRIAMYCIN™, gamma interferon, bacterial byproducts such as lipopolysaccharides, mycobacterial antigens such as BCG, a UCP expression vector, a TCRαβ engagement molecule and a fatty acid.

Please replace the paragraph beginning on page 8, line 28 with the following amended paragraph: 5/5/08 T.T.

The metabolic modifying agent is added to the tumor cell to induce coupling of electron transport and oxidative phosphorylation. Preferably the metabolic modifying agent is selected from the group consisting of glucose, phorbol myristate acetate in combination with ionomycin, MHC class II HLA-DP/DQ ligand, GDP, CD40 binding peptide, UCP antisense, dominant negative UCP, sodium acetate, and staurosporine. Once electron transport is coupled to oxidative phosphorylation, Fas expression is induced on the cell surface and a apoptotic chemotherapeutic agent can be added to induce apoptosis of the tumor cell. In one embodiment the apoptotic chemotherapeutic agent is selected from the group consisting of ADRIAMYCIN™, cytarabine, doxorubicin, and methotrexate.

Please replace the paragraph beginning on page 11, line 19 with the following amended paragraph: 5/5/08 T.T.

According to yet another aspect of the invention a method for inducing pancreatic β cell death in a Type II diabetic is provided. The method includes the steps of contacting a pancreatic β cell of a Type II diabetic with an amount of an MHC class II HLA-DR inducing agent effective to induce the expression of the MHC class II HLA-DR on the surface of the pancreatic β cell, and selectively engaging the MHC class II HLA-DR by contacting the cell with an MHC class II HLA-DR ligand effective to induce pancreatic β cell death. The MHC class II HLA-DR inducing agent is selected from the group consisting of ADRIAMYCIN™, gamma interferon, bacterial byproducts such as lipopolysaccharides, mycobacterial antigens such as BCG, a UCP expression vector, a TCRαβ engagement molecule and a fatty acid in one embodiment.

Please replace the paragraph beginning on page 15, line 3 with the following amended paragraph: 5/5/08 T.T.

In another aspect the invention is a composition of a metabolic modifying agent and an apoptotic chemotherapeutic agent. Preferably the metabolic modifying agent is selected from the group consisting of glucose, phorbol myristate acetate in combination with ionomycin, MHC class II HLA-DP/DQ ligand, GDP, CD40 binding peptide, sodium acetate, UCP antisense, dominant negative UCP,, and staurosporine. In a preferred embodiment the apoptotic chemotherapeutic agent is selected from the group consisting of ADRIAMYCIN™, cytarabine, doxorubicin, and methotrexate.

Please replace the paragraph beginning on page 15, line 13 with the following amended paragraph: 5/5/08 T.T.

The invention according to another aspect is a composition of an MHC class II HLA-DR inducing agent and an MHC class II HLA-DR ligand. In one embodiment the MHC class II HLA-DR inducing agent is selected from the group consisting of ADRIAMYCIN™, gamma interferon, bacterial byproducts such as lipopolysaccharides, mycobacterial antigens such as BCG, a UCP expression vector, a TCRαβ engagement molecule and a fatty acid. In another embodiment the MHC class II HLA-DR ligand is selected from the group consisting of an anti-MHC class II HLA-DR antibody, CD4 molecules, αβ T cell receptor molecules, γδ T cell receptor molecules and a

MHC class II HLA-DR binding peptide. According to yet another embodiment the MHC class II HLA-DR inducing agent and the MHC class II HLA-DR ligand are present in an amount effective to lyse a tumor cell. The composition may be formulated in a pharmaceutically acceptable carrier.

Please replace the paragraph beginning on page 16, line 6/1 with the following amended paragraph: 5/5/08 T.T.

In some embodiments the B7 inducing agent is ADRIAMYCIN™, gamma interferon, a fatty acid, a lipoprotein, an anti-MHC class II HLA-DR antibody, a MHC class II HLA-DR binding peptide, a B7 expression vector, or a UCP expression vector.

Please replace the paragraph beginning on page 17, line 12/13 with the following amended paragraph: 5/5/08 T.T.

In some embodiments the B7 inducing agent is ADRIAMYCIN™, gamma interferon, bacterial byproducts such as lipopolysaccharides and lipoproteins, mycobacterial antigens such as BCG, and fatty acids, an anti-MHC class II HLA-DR antibody, a MHC class II HLA-DR binding peptide, a B7 expression vector, or a UCP expression vector. In other embodiments the CD28 inducing agent is a T cell receptor engagement molecule, CD3 engagement molecule, IL4, or a CD28 expression vector. In yet another embodiment the composition also includes a pharmaceutically acceptable carrier.

Please replace the paragraph beginning on page 18, line 2/3 with the following amended paragraph: 5/5/08 T.T.

In some embodiments the B7 inducing agent is ADRIAMYCIN™, gamma interferon, bacterial byproducts such as lipopolysaccharides and lipoproteins, mycobacterial antigens such as BCG, and fatty acids, an anti-MHC class II HLA-DR antibody, a MHC class II HLA-DR binding peptide, a B7 expression vector, or a UCP expression vector.

Please replace the paragraph beginning on page 24, line 12/14 with the following amended paragraph: 5/5/08 T.T.

In the aspects of the invention that the mammalian cell is a tumor cell and the cell is only treated with an MHC class II HLA-DR inducing agent but not an MHC class II HLA-DR ligand the MHC class II HLA-DR inducing agent does not include ADRIAMYCIN™ and gamma interferon. When the MHC class II HLA-DR inducing agent is ADRIAMYCIN™ or gamma interferon the method of lysing the tumor cell requires the additional step of contacting the tumor cell with an MHC class II HLA-DR ligand to cause cell lysis.

Please replace the paragraph beginning on page 24, line 19 with the following amended paragraph: 5/5/08 T.T.

As used herein an "MHC class II HLA-DR inducing agent" is an agent which causes MHC class II HLA-DR to be expressed on the cell surface. Preferably the MHC class II HLA-DR inducing agent is a pharmacological agent that causes uncoupling of electron transport and oxidative phosphorylation, resulting in reduced mitochondrial membrane potential within the cell. MHC class II HLA-DR inducing agents include but are not limited to ADRIAMYCIN™, gamma interferon, bacterial byproducts such as lipopolysaccharides, mycobacterial antigens such as BCG, a UCP expression vector, a TCRαβ engagement molecule and a fatty acid. Although gamma interferon induces expression of both MHC class II HLA-DR and MHC class II HLA-DP/DQ it can still be used in combination with an MHC class II HLA-DR ligand which selectively binds to MHC class II HLA-DR and not MHC class II HLA-DP/DQ. The MHC class II HLA-DR inducing agent is an isolated molecule. An isolated molecule is one which has been removed from its natural surroundings and formulated for administration to an organism. ADRIAMYCIN™, gamma interferon, bacterial byproducts such as lipopolysaccharides, mycobacterial antigens such as BCG are all well known compounds which can be purchased from a variety of commercial sources. UCP expression vector can be prepared by methods well known in the art, such methods are described in detail below. Fatty acids are also well known compounds that can be purchased commercially from many sources. Preferred fatty acids include but are not limited to oleic acid, palmitate, and myristic acid. A "TCRαβ engagement molecule" as used herein refers to any compound that can bind to and cause cell surface crosslinking of CD4 and the αβT cell receptor (αβTCR). Such compounds are known in the art. For instance heterobifunctional antibodies are capable of crosslinking CD4

and αβTCR by interacting with both molecules on the surface of the cell. Other CD4/αβTCR binding molecules can be identified with routine experimentation and are also encompassed by the term TCRαβ engagement molecule. Routine screening methods for identifying such binding molecules are set forth below.

Please replace the paragraph beginning on page 29, line 16 with the following amended paragraph:

9/5/08 T.T.

An "apoptotic chemotherapeutic agent" as used herein is a group of molecules which function by a variety of mechanisms to induce apoptosis in rapidly dividing cells. Apoptotic chemotherapeutic agents are a class of chemotherapeutic agents which are well known to those of skill in the art. Chemotherapeutic agents include those agents disclosed in Chapter 52, Antineoplastic Agents (Paul Calabresi and Bruce A. Chabner), and the introduction thereto, 1202-1263, of Goodman and Gilman's "The Pharmacological Basis of Therapeutics", Eighth Edition, 1990, McGraw-Hill, Inc (Health Professions Division), incorporated herein by reference. Suitable chemotherapeutic agents may have various mechanisms of action. The classes of suitable chemotherapeutic agents include (a) Alkylating Agents such as nitrogen mustard (e.g. mechlorethamine, cylophosphamide, ifosfamide, melphalan, chlorambucil), ethylenimines and methylmelamines (e.g. hexamethylmelamine, thiotepa), alkyl sulfonates (e.g. busulfan), nitrosoureas (e.g. carmustine which is also known as BCNU, lomustine which is also known as CCNU semustine which is also known as methyl-CCNU, chlorozoticin, streptozocin), and triazines (e.g. dicarbazine which is also known as DTIC); (b) Antimetabolites such as folic acid analogs (e.g. methotrexate), pyrimidine analogs (e.g. 5-fluorouracil floxuridine, cytarabine, and azauridine and its prodrug form azaribine), and purine analogs and related materials (e.g. 6-mercaptopurine, 6-thioguanine, pentostatin); (c) Natural Products such as the vinca alkaloids (e.g. vinblastine, Vincristine), epipodophylotoxins (e.g. etoposide, teniposide), antibiotics (.e.g dactinomycin which is also known as actinomycin-D, daunorubicin, doxorubicin, bleomycin, plicamycin, mitomycin, epirubicin, which is 4-epidoxorubicin, idarubicin which is 4-dimethoxydaunorubicin, and mitoxanthrone), enzymes (.e.g L-asparaginase), and biological response modifiers (e.g. Interferon alfa); (d) Miscellaneous Agents such as the platinum coordination complexes (e.g. cisplatin,

carboplatin), substituted ureas (e.g. hydroxyurea), methylhydiazine derivatives (e.g. procarbazine), adreocortical suppressants (e.g. mitotane, aminoglutethimide) TAXOL™; (e) Hormones and Antagonists such as adrenocorticosteroids (e.g. prednisone or the like), progestins (e.g. hydroxyprogesterone caproate, medroxyprogesterone acetate, megestrol acetate), estrogens (e.g. diethyestilbestrol, ethinyl estradiol, and the like), antiestrogens (e.g. tamoxifen), androgens (e.g. testosterone propionate, fluoxymesterone, and the like), antiandrogens (e.g. flutamide); and gonadotropin-releasing hormone analogs (e.g. leuprolide) and (F) DNA damaging compounds such as ADRIAMYCIN™.

Please replace the paragraph beginning on page 41, line 25 with the following amended paragraph: 5/5/08 T.T.

As used herein "B7 inducing agent" is an agent which causes B7 (and other related family members retaining sequence homology with B7) to be expressed on a nerve cell surface. In one preferred embodiment the B7 inducing agent is a pharmacological agent that causes dissipation of proton motor force such as by uncoupling of electron transport and oxidative phosphorylation, resulting in reduced mitochondrial membrane potential within the cell. B7 inducing agents which cause dissipation of the proton motor force include but are not limited to ADRIAMYCIN™, gamma interferon, bacterial byproducts such as lipopolysaccharides, lipoproteins BCG, fatty acids, cAMP inducing agents and a UCP expression vector. A "cAMP inducing agent" as used herein is any compound which elevates intracellular levels of cAMP. Such compounds include but are not limited to isoproterenol, epinephrine, norepinephrine, phosphodiester inhibitors, theophylline, and caffeine. In another preferred embodiment the B7 inducing agent is a B7 expression vector. Such a vector can be stably expressed in the nerve cell to produce B7 which can be expressed on the cell surface. The B7 inducing agent is an isolated molecule. An isolated molecule is one which has been removed from its natural surroundings and formulated for administration to an organism.

Please replace the paragraph beginning on page 70, line 22 with the following amended paragraph: 5/5/08 T.T.

1. Resistance to apoptosis is characterized by failure to express Fas: The cell lines utilized herein include L1210, a leukemic cell line; HL60, a human pro-myelocytic cell line; and PC12, a pheochromocytoma cell line which can be induced to differentiate into a neuronal cell line in the presence of NGF (Lindenboim, L, et al., *Cancer Res*, 1995, 55:1242-7). Each cell line was examined in parallel with apoptotic resistant sublines: L1210 DDP, HL60 MDR, and PC12Trk. L1210 DDP are resistant to cisplatin and methotrexate; HL60 MDR are resistant to ADRIAMYCIN™ induced apoptosis; PC12 TrkA, which have been transfected with TrkA which results in constitutively expression the NGF receptors, are not susceptible to alcohol and NGF withdrawal as are the PC12 cells.

Please replace the paragraph beginning on page 74, line 21 with the following amended paragraph: 5/5/08 I.T.

4. Treatment of L1210 DDP cells with staurosporine restores Fas expression and susceptibility to drug-induced apoptosis: L1210, but not L1210 DDP, undergo apoptotic cell death. We treated L1210 or L1210 DDP cells with the staurosporine, which inhibits protein kinase C and *increases mitochondrial membrane potential*, or an anti-cancer agent to which both cells are sensitive, ADRIAMYCIN™. Fas expression was increased or induced on both L1210 and L1210 DDP, respectively, in the presence of staurosporine or ADRIAMYCIN™ (Figure 3). The L1210 DDP changed morphologically and began to divide rapidly, changes which appeared to correspond with a reversion back to the phenotype of the L1210 cells. These results demonstrate that Fas expression results in parallel with altered metabolic activity.